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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,680	01/09/2002	Hans-Peter Schwarz	R-222.00	7064

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EXAMINER	
WAX, ROBERT A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 04/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/831,680	SCHWARZ ET AL.	
	Examiner	Art Unit	
	Robert A. Wax	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *6* is/are allowed.

6)☒ Claim(s) *1-5,7,8,10 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. All previous rejections are hereby withdrawn in view of the Applicant's arguments, see pages 4-8 of the applicants' response, filed January 29, 2004, with respect to the rejection of claim 2 under 35 USC 112, second paragraph and with respect to the rejection of claims 1-3, 7 and 11 under 35 USC 103(a) have been fully considered and are persuasive. Therefore, the rejections have been withdrawn. However, upon further consideration, new grounds of rejection are made under 35 USC 112, first paragraph, both written description and enablement.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-5, 7, 8, 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to pharmaceutical preparations containing a RAP mutant or a RAP analogue. The claims do not require that the mutant or analogue possess any particular conserved structure, or other distinguishing feature, such as a specific biological activity. Thus, the claims are drawn to a genus of polypeptides that is defined by an unclear functional relationship to RAP. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claim that is sufficiently disclosed is a partial structure in the form of a recitation of percent identity. The specification does not identify any particular portion of the structure that must be characteristic of the claimed genus are not described. The specification does not identify any particular amino acids that should be mutated, nor is there any disclosure of other compounds that could be considered RAP analogues. The only adequately described species is full-length RAP. The specification does discuss particular fragments in paragraph 0021 and claims limited to such fragments would not lack adequate written description. Accordingly, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the

"written description" inquiry, whatever is now claimed." (See page 1117.) The specification does not it clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116), As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers* v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird,* 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF' s were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Therefore, only amino acid designated by SEQ ID NO: 2, but not the full breadth of the claim meets the written description provision of 35 U. S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision.

4. Claims 1-5, 7, 8, 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for pharmaceutical compositions as claimed that include full-length RAP, does not reasonably provide enablement for RAP mutants or RAP analogues. The specification does not enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The criteria for determining undue experimentation, summarized in *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988), are: 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in that art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims. The factors will be analyzed for the mutants and analogues separately, beginning with the mutants.

The instant claims are drawn to, *inter alia*, pharmaceutical compositions containing mutants of RAP. The specification mentions "mutants" of RAP in paragraph 0016 and permits their inclusion "as long as they may be used in the treatment of blood coagulation disorders and may bind to a receptor functionally, i.e., competitively." Thus, the only definition of a mutant RAP is one that may be used in the treatment of blood coagulation disorders and may competitively bind to a receptor. One definition of a mutant is a protein that has been altered by substitution, deletion and insertion of one or more amino acids.

In the instant case, 1) the quantity of experimentation necessary is very large since the number of possible mutants is enormous; 2) the amount of direction or guidance presented is zero. In order to predict with reasonable assurance the effect that different deletion, substitution and/or insertion mutations are likely to have on the protein, and thereby predict which mutants will retain biological activity, the skilled

artisan would require data regarding, for example, the molecular basis of the protein's activity, its secondary and tertiary structure and the relative importance of any domains of the protein in maintaining said activity. The instant specification provides no such information. Continuing with the factors, 3) the specification contains no working examples of RAP mutants, 4) the nature of the invention is a synergistic combination of ingredients for treatment of blood coagulation disorders, one of the ingredients is RAP, 5) the prior art does not teach such compositions, 6) the relative skill of those in the art is very high, that of a PhD-level investigator, 7) the predictability of the art is low since the specification provides no information regarding, for example, the domain structure of the protein, the location of the active site, or sites of interaction with other proteins, cofactors or regulatory molecules. Possession of this information would increase the level of predictability, and 8) the breadth of the claims is very large since the number of possible proteins falling within the definition of mutant RAP is so large.

In view of this analysis, particularly, the amount of experimentation required, the lack of guidance and the low predictability of which of the myriad possible deletion, substitution and insertion mutants of RAP would be likely to retain the named biological activity, the conclusion that it would require undue experimentation to practice the invention with regard to RAP mutants in inescapable.

The instant claims are also drawn to, *inter alia*, pharmaceutical compositions containing analogues of RAP. The specification mentions "analogues" of RAP in paragraph 0016 and permits their inclusion "as long as they may be used in the treatment of blood coagulation disorders and may bind to a receptor functionally, i.e.,

competitively." Thus, the only definition of a RAP analogue is one that may be used in the treatment of blood coagulation disorders and may competitively bind to a receptor. There are many different definitions of an analogue but the broadest would include any protein that could be considered to have any relationship whatsoever to RAP. This would therefore include any other human protein, any protein that has a similar molecular weight, etc., with no requirement that the protein have the same activity as RAP.

In the instant case, 1) the quantity of experimentation necessary is very large since the number of possible analogues is enormous; 2) the amount of direction or guidance presented is zero. In order to predict with reasonable assurance which analogues will have the named biological activity, the skilled artisan would require data regarding, for example, the molecular basis of the protein's activity, its secondary and tertiary structure and the relative importance of any domains of the protein in maintaining said activity. The instant specification provides no such information. Continuing with the factors, 3) the specification contains no working examples of RAP analogues, 4) the nature of the invention is a synergistic combination of ingredients for treatment of blood coagulation disorders, one of the ingredients is RAP, 5) the prior art does not teach such compositions, 6) the relative skill of those in the art is very high, that of a PhD-level investigator, 7) the predictability of the art is low since the specification provides no information regarding, for example, the domain structure of the protein, the location of the active site, or sites of interaction with other proteins, cofactors or regulatory molecules. Possession of this information would increase the

level of predictability, and 8) the breadth of the claims is very large since the number of possible proteins falling within the definition of "RAP analogue" is so large.

In view of this analysis, particularly, the amount of experimentation required, the lack of guidance and the low predictability of which of the RAP analogues would be likely to have the named biological activity, the conclusion that it would require undue experimentation to practice the invention with regard to RAP analogues in inescapable.

Conclusion

5. An amendment to claim 1 deleting "a RAP mutant, a RAP analogue" and inserting "a RAP fragment comprising the domain which keeps proteins from binding to LRP" would be enabled and possess adequate written description and be allowable. Until such amendment is filed, only claim 6 is allowable.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Wax whose telephone number is (571) 272-0623. The examiner can normally be reached on Monday through Friday, between 9:00 AM and 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S. F. Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert A. Wax
Primary Examiner
Art Unit 1653